```
=> File .Biotech
=> s (Factor VIII or FVIII or Factor 8)
L1       58450 (FACTOR VIII OR FVIII OR FACTOR 8)

=> s l1 and (blood(l)coagul?)
L2       13760 L1 AND (BLOOD(L) COAGUL?)

=> s l2 and (Willebrand factor or vWF)
L3        3104 L2 AND (WILLEBRAND FACTOR OR VWF)

=> s l3 and (prepar? or purif? or recover? or immunopurif? or affinity purif?)
L4        1236 L3 AND (PREPAR? OR PURIF? OR RECOVER? OR IMMUNOPURIF? OR AFFINI
               TY PURIF?)

=> s l4 and (filter? or filtr?)
L5         570 L4 AND (FILTER? OR FILTR?)

=> s l5 and (pore or porus)
L6         260 L5 AND (PORE OR PORUS)

=> s l5 and (pore or porous)
L7         293 L5 AND (PORE OR POROUS)

=> s l7 and(ultrafiltr? or diafiltr? or nanofiltr?)
L8         105 L7 AND(ULTRAFILTR? OR DIAFILTR? OR NANOFILTR?)

=> s l8 and (Ca or Ca2 or calcium or CaCl2 or Calcium Chloride)
L9         102 L8 AND (CA OR CA2 OR CALCIUM OR CACL2 OR CALCIUM CHLORIDE)

=> s l9 and (dissociat? or ion exchange chromatograh?)
L10         84 L9 AND (DISSOCIAT? OR ION EXCHANGE CHROMATOGRAH?)

=> s l10 and (cryoprecipitat? or haparin precipitat?)
L11          1 L10 AND (CRYOPRECIPITAT? OR HAPARIN PRECIPITAT?)

=> d l11 bib ab

L11  ANSWER 1 OF 1  USPATFULL on STN
AN     85:4746  USPATFULL
TI     Preparation of highly purified human antihemophilic
       factor
IN     Chavin, Stephen I., Rochester, NY, United States
       Fay, Philip J., Rochester, NY, United States
PA     University of Rochester, Rochester, NY, United States (U.S. corporation)
PI     US 4495175              19850122
AI     US 1982-405456          19820805 (6)
DT     Utility
FS     Granted
EXNAM  Primary Examiner: Rosen, Sam
LREP   Aston, David J., Leitereg, Theodore J.
CLMN   Number of Claims: 10
ECL    Exemplary Claim: 1,7
DRWN   5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 512
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     Highly purified, biologically active Human Antihemophilic
       Factor (AHF) preparations are prepared having
       specific activities of about 4000-8000 units per milligram of AHF. In
       the method of preparation an AHF concentrate, prepared
       by fractionation of plasma to partially remove fibrinogen, fibronectin
       and other plasma components is subjected to a separation on the basis of
       Stokes' radius to separate AHF from the bulk of remaining proteins in
       the AHF concentrate. The pooled fractions containing AHF activity are
       concentrated by precipitation with ammonium sulfate, sodium sulfate,
       etc., by diafiltration, by PEG addition, or the like. The
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concentrate, is solubilized or equilibrated in an aqueous medium and treated to change the effective Stokes' radius of the AHF to an apparently low value and then subjected to a separation from the concentrate. The AHF pool from above is treated to remove cations by dialysis against an appropriate buffer of lower ionic strength and chromatographed on an anion-exchange medium. The AHF fraction from the above chromatography, is a highly **purified** AHF **preparation.**

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=> s l10 and (solvent or detergent)
L12         81 L10 AND (SOLVENT OR DETERGENT)

=> s l12 and (CHTOUROU A? or NOGRE M? or PORTE P?)/au
L13          0 L12 AND (CHTOUROU A? OR NOGRE M? OR PORTE P?)/AU

=> s CHTOUROU, A?/au
L14         25 CHTOUROU, A?/AU

=> s l12 and l14
L15          0 L12 AND L14

=> s l14 and (Factor VIII or FVIII solution)
L16          6 L14 AND (FACTOR VIII OR FVIII SOLUTION)

=> s l12 and l16
L17          0 L12 AND L16

=> s NOGRE, M?/au
L18          2 NOGRE, M?/AU

=> d l18 1-2 bib ab

L18  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1999:404998  CAPLUS
DN   131:49441
TI   Method for preparing virus-free factor VIII solution by filtration
IN   Chtourou, Abdessatar; Nogre, Michel; Porte, Pierre
PA   Laboratoire Francais du Fractionnement et des Biotechnologies, Fr.
SO   PCT Int. Appl., 30 pp.
     CODEN: PIXXD2
DT   Patent
LA   French
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   WO 9931138          A1   19990624      WO 1998-FR2715   19981214
         W:  AU, CA, JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     FR 2772381          A1   19990618      FR 1997-15888    19971215
     FR 2772381          B1   20010608
     CA 2314610          AA   19990624      CA 1998-2314610  19981214
     AU 9915681          A1   19990705      AU 1999-15681    19981214
     AU 752271           B2   20020912
     EP 1037923          A1   20000927      EP 1998-959975   19981214
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 2002508396       T2   20020319      JP 2000-539061   19981214
PRAI FR 1997-15888       A    19971215
     WO 1998-FR2715      W    19981214
AB   The invention concerns a method for preparing by filtration a factor VIII
     solution which is essentially free of virus and high mol. weight vWF.  The
     method comprises preparing a solution containing high or very high purity
factor
```

VIII essentially free of high mol. weight VIII-vWf complexes and filtering the solution with a hydrophilic filter with porosity as low as 15 nm, such as Planova 15N (Asahi Chemical). Chaotropic ions, such as provided by CaCl2, may be used to effectuate the dissociation The type of divalent ion and its concentration affected the yield. 0.35M CaCl2 is preferred. Both filtration pressure and temperature were found to affect the yield: pressure less than that
recommended by the manufacturer is used and the temperature is advantageously about 35°.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 2 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-360082 [31] WPIDS
DNC C1999-106780
TI Removing viruses from factor VIII solution - by filtration on nanoporous hydrophilic filter.
DC B04
IN CHTOUROU, A; **NOGRE, M**; PORTE, P; CHTOUROU, A S
PA (FRFR-N) LAB FR DU FRACTIONNEMENT & BIOTECHNOLOGI
CYC 23
PI FR 2772381 A1 19990618 (199931)* 24
WO 9931138 A1 19990624 (199932) FR
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9915681 A 19990705 (199948)
EP 1037923 A1 20000927 (200048) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002508396 W 20020319 (200222) 27
AU 752271 B 20020912 (200264)
ADT FR 2772381 A1 FR 1997-15888 19971215; WO 9931138 A1 WO 1998-FR2715 19981214; AU 9915681 A AU 1999-15681 19981214; EP 1037923 A1 EP 1998-959975 19981214, WO 1998-FR2715 19981214; JP 2002508396 W WO 1998-FR2715 19981214, JP 2000-539061 19981214; AU 752271 B AU 1999-15681 19981214
FDT AU 9915681 A Based on WO 9931138; EP 1037923 A1 Based on WO 9931138; JP 2002508396 W Based on WO 9931138; AU 752271 B Previous Publ. AU 9915681, Based on WO 9931138
PRAI FR 1997-15888 19971215
AB FR 2772381 A UPAB: 20021105
Process for preparing a virus-safened solution of factor VIII (FVIII) containing no high-molecular-weight von Willebrand factor (vWF) comprises (a) preparing a high-purity FVIII solution containing or not containing high-molecular-weight vWF-FVIII complexes, (b) dissociating any high-molecular-weight vWF-FVIII complexes in the solution, and (c) filtering the solution on a hydrophilic filter having a pore size as low as 15 nm.
USE - for treating haemophilia A.
ADVANTAGE - The process removes both high-molecular-weight vWF and viruses, including small viruses such as parvovirus B19.
Dwg.0/1

=> s PORTE, P?/au
L19 126 PORTE, P?/AU

=> s l12 and l19
L20 0 L12 AND L19

=> s l19 and (Factor VIII or FVIII solution)
L21 10 L19 AND (FACTOR VIII OR FVIII SOLUTION)

=> s l16 or l18 or l21 and (filtr? or filter? factor VIII or FVIII)
L22 6 L16 OR L18 OR L21 AND (FILTR? OR FILTER? FACTOR VIII OR FVIII
)

=> Dup rem L22
PROCESSING COMPLETED FOR L22
L23 4 DUP REM L22 (2 DUPLICATES REMOVED)

=> d l23 1-4 bib ab

L23 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:404998 CAPLUS
DN 131:49441
TI Method for preparing virus-free **factor VIII** solution by **filtration**
IN **Chtourou, Abdessatar**; **Nogre, Michel**; **Porte, Pierre**
PA Laboratoire Francais du Fractionnement et des Biotechnologies, Fr.
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9931138	A1	19990624	WO 1998-FR2715	19981214
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2772381	A1	19990618	FR 1997-15888	19971215
	FR 2772381	B1	20010608		
	CA 2314610	AA	19990624	CA 1998-2314610	19981214
	AU 9915681	A1	19990705	AU 1999-15681	19981214
	AU 752271	B2	20020912		
	EP 1037923	A1	20000927	EP 1998-959975	19981214
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002508396	T2	20020319	JP 2000-539061	19981214
PRAI	FR 1997-15888	A	19971215		
	WO 1998-FR2715	W	19981214		

AB The invention concerns a method for preparing by **filtration** a **factor VIII** solution which is essentially free of virus and high mol. weight vWF. The method comprises preparing a solution containing high or very high purity **factor VIII** essentially free of high mol. weight VIII-vWf complexes and filtering the solution with a hydrophilic filter with porosity as low as 15 nm, such as Planova 15N (Asahi Chemical). Chaotropic ions, such as provided by CaCl2, may be used to effectuate the dissociation The type of divalent ion and its concentration affected the yield. 0.35M CaCl2 is preferred. Both **filtration** pressure and temperature were found to affect the yield: pressure less than that recommended by the manufacturer is used and the temperature is advantageously about 35°.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 4 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-360082 [31] WPIDS
DNC C1999-106780
TI Removing viruses from **factor VIII** solution - by **filtration** on nanoporous hydrophilic filter.
DC B04
IN **CHTOUROU, A**; **NOGRE, M**; **PORTE, P**; **CHTOUROU, A S**
PA (FRFR-N) LAB FR DU FRACTIONNEMENT & BIOTECHNOLOGI
CYC 23
PI FR 2772381 A1 19990618 (199931)* 24
WO 9931138 A1 19990624 (199932) FR

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9915681 A 19990705 (199948)
EP 1037923 A1 20000927 (200048) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002508396 W 20020319 (200222) 27
AU 752271 B 20020912 (200264)
ADT FR 2772381 A1 FR 1997-15888 19971215; WO 9931138 A1 WO 1998-FR2715 19981214; AU 9915681 A AU 1999-15681 19981214; EP 1037923 A1 EP 1998-959975 19981214, WO 1998-FR2715 19981214; JP 2002508396 W WO 1998-FR2715 19981214, JP 2000-539061 19981214; AU 752271 B AU 1999-15681 19981214
FDT AU 9915681 A Based on WO 9931138; EP 1037923 A1 Based on WO 9931138; JP 2002508396 W Based on WO 9931138; AU 752271 B Previous Publ. AU 9915681, Based on WO 9931138
PRAI FR 1997-15888 19971215
AB FR 2772381 A UPAB: 20021105
Process for preparing a virus-safened solution of **factor VIII** (**FVIII**) containing no high-molecular-weight von Willebrand factor (vWF) comprises (a) preparing a high-purity **FVIII solution** containing or not containing high-molecular-weight vWF-**FVIII** complexes, (b) dissociating any high-molecular-weight vWF-**FVIII** complexes in the solution, and (c) filtering the solution on a hydrophilic filter having a pore size as low as 15 nm.
USE - for treating haemophilia A.
ADVANTAGE - The process removes both high-molecular-weight vWF and viruses, including small viruses such as parvovirus B19.
Dwg.0/1

L23 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN 1992:67159 CAPLUS
DN 116:67159
TI Method for preparing high-purity **factor VIII** including a rapid immunoadsorption step
IN **Chtourou, Abdessatar**
PA Fondation Nationale de Transfusion Sanguine, Fr.
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9118017	A1	19911128	WO 1991-FR400	19910517
W: CA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
FR 2662166	A1	19911122	FR 1990-6252	19900518
PRAI FR 1990-6252		19900518		

AB A method for preparing high-purity **Factor VIII** from a complex aqueous mixture containing von Willebrand Factor-complexed **Factor VIII** includes immunoadsorption on an anti-**Factor VIII** monoclonal antibody. The method is characterized in that (a) a sufficient quantity of divalent ions is added to the complex aqueous mixture to ensure the dissociation of the **Factor VIII**/von Willebrand Factor complex; (b) the mixture containing **Factor VIII** is contacted with an immunoadsorbent consisting of an anti-**Factor VIII** monoclonal antibody which is immobilized on a rigid support by a covalent bond, the monoclonal antibody being so selected that it is directed against the light chain of the **Factor VIII** and can both inhibit the coagulative activity of the **Factor VIII**:C and bond the **Factor VIII** through strong hydrophobic interactions; and (c) the immunoadsorbent **Factor VIII** solution is eluted. **Factor VIII** was purified from cryopptd. blood plasma by treatment with

CaCl2 and viral inactivation solution, immunoadsorption on monoclonal antibody 463A8-Sephacryl S1000 gel, elution with buffer containing Tween 80, and ion exchange chromatog. on Q Sepharose FF. The 463A8 antibody was prepared by standard hybridoma methods.

L23 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
AN 1991:614824 CAPLUS
DN 115:214824
TI Concentrated solutions of blood coagulation **factor VIII**
IN **Chtourou, Abdessatar**
PA Fondation Nationale de Transfusion Sanguine, Fr.
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9113625	A1	19910919	WO 1991-FR211	19910315
	W: US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	FR 2659557	A1	19910920	FR 1990-3328	19900315
	FR 2665364	A2	19920207	FR 1990-9828	19900801
	EP 472711	A1	19920304	EP 1991-906628	19910315
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
PRAI	FR 1990-3328		19900315		
	FR 1990-9828		19900801		
	WO 1991-FR211		19910315		

AB Concentrate **factor VIII** solns. of intermediate purity are prepared from cryoppts. by controlled double precipitation, in order to remove the undesired proteins in 2 stages. Human blood plasma cryoppt. (20 g) was dissolved in 4 times its volume of 20 mM tris-HCl buffer (pH 7). The pH was adjusted to 7.1 (0.5N HAcO), followed by treatment with 24 units heparin/mL, centrifugation, treatment of the supernatant with Al(OH)3 (110 g/1 kg cryoppt.), pH adjustment to 6 with 0.5N HAcO, and centrifugation, to give the **factor VIII** concentrate

=> s l12 and l23
L24 0 L12 AND L23

=> s l23 and (Ca or Ca2 or Calcium or CaCl2 or Calcium Chloride)
L25 2 L23 AND (CA OR CA2 OR CALCIUM OR CACL2 OR CALCIUM CHLORIDE)

---Logging off of STN---

ENTER ANSWER NUMBER OR RANGE (1):END

=>
Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 14:46:59 ON 22 JUN 2004